1 : *J Exp Med* 1995 Feb 1;181(2):631-40

Related Articles, Books, LinkOut

PubMed Services

Related Resources

Antagonists of monocyte chemoattractant protein 1 identified by modification of functionally critical NH2-terminal residues.

Gong JH, Clark-Lewis I

Biomedical Research Centre, University of British Columbia, Vancouver, Canada.

Monocyte chemoattractant protein (MCP)-1 analogues were designed to determine the role of the NH2-terminal region in structure and function. The NH2-terminal residue was important for function and receptor binding, as it could not be deleted or extended. However the NH2-terminal pyroglutamate residue of the wild type was not essential as it could be replaced by several other noncyclic amino acids without loss of activity. Residues 7-10 were essential for receptor desensitization, but were not sufficient for function, and the integrity of residues 1-6 were required for functional activity. A peptide corresponding to MCP-1, 1-10 lacked detectable receptor-binding activities, indicating that residues 1-10 are essential for MCP-1 function, but that other residues are also involved. Several truncated analogues, including 8-76, 9-76, and 10-76, desensitized MCP-1-induced Ca2+ induction, but were not significantly active. These analogues were antagonists of MCP-1 activity with the most potent being the 9-76 analogue (IC50 = 20 nM) The 9-76 specifically bound to MCP-1 receptors with a Kd of 8.3 nM, which was three-fold higher than MCP-1 (Kd 2.8 nM). The 9-76 analogue desensitized the Ca2+ response to MCP-1 and MCP-3, but not to other CC chemokines, suggesting that it is MCP receptor specific. The availability of these compounds will be helpful in evaluating MCP receptor antagonists as anti-inflammatory therapeutics.

PMID: 7836918, UI: 95138695

Display Abstract Save Text Add to Clipboard

Revised: January 10, 2000.

jmurphy3

HPS Trailer Page
for
WEST

Printer: cm1_9e12_gbefptr

Summary

Document	Pages	Printed	Missed
FR002744730A1	37	37	0
Total (1)	37	37	0